mesoblast
the regenerative medicine company

asx announcement

Rheumatoid Arthritis New Major Clinical Target After Mesoblast Obtains Positive Results in Inflammatory Arthritis

Key Points:

- Intravenous injection of Mesenchymal Precursor Cells (MPCs) resulted in selective migration to inflamed joints and lymph nodes in a sheep model of Rheumatoid Arthritis (RA)
- A single intravenous injection of allogeneic, or "off-the-shelf", MPCs significantly reduced synovial tissue levels of TNF-alpha, IL-6, and IL-17, and reduced mononuclear cell infiltration
- Reduced cytokine and inflammatory cell levels were accompanied by significant reduction in pathology severity scores and synovial hyperplasia
- MPCs may have a mechanism of action that is unique from other biological therapies by shutting down multiple cytokine pathways simultaneously
- MPCs could be a safe, first line therapy to induce sustained improvement of joint inflammation in RA
- Phase 2 clinical trial in RA expected to commence Q4 2012
- RA is the second clinical indication, after type 2 diabetes, to be targeted using Mesoblast's intravenous product formulation

Melbourne, Australia; 24 July 2012: Regenerative medicine company Mesoblast Limited (ASX:MSB) today announced positive results in a large animal model of Rheumatoid Arthritis (RA) following a single intravenous injection of its proprietary allogeneic, or "off-the-shelf", immunomodulatory adult Mesenchymal Precursor Cells (MPCs).

Mesoblast Chief Executive Professor Silviu Itescu said that the results indicated that the Company's immunomodulatory MPCs may have a mechanism of action that is unique from other biological therapies by shutting down multiple cytokine pathways simultaneously, and that this could become a first line treatment with a superior and sustained benefit on reducing inflammation and destruction of joints in people suffering from severe RA.

RA is an autoimmune disease driven and perpetuated by pro-inflammatory cytokines such as TNF-alpha, IL-6, and IL-17. Treatments targeting any of these pathways alone are only moderately effective in RA, need to be administered chronically, and may cause unacceptable infectious adverse events. A single intravenous injection of allogeneic MPCs in sheep with collagen-induced arthritis concomitantly affected T cells, monocytes/macrophages, and synoviocytes to simultaneously shut down TNF-alpha, IL-6, and IL-17 cytokine pathways, and improve joint pathology.

asx announcement

Severe joint synovial inflammation with cartilage loss and bony erosions, characteristic of human RA, occurs in sheep injected with collagen. In a pilot study, significant numbers of allogeneic MPCs were detected in involved joints or lymph nodes of arthritic sheep at 24 hours after a single intravenous injection, but not in normal sheep, indicating that MPCs selectively migrate to sites of immune-mediated inflammation.

A randomized, placebo-controlled study was next performed in 30 sheep with established collagen-induced arthritis, comparing a single intravenous injection of allogeneic MPCs at one of three doses (0.3, 1 and 2 million MPCs/kg) to saline. Thirty days later, joint synovial tissues from arthritic sheep were examined. In comparison with saline treated controls, synovial tissue from arthritic sheep receiving a single intravenous injection of 2 million MPCs/kg showed 88% mean reduction in IL-6 levels ($p=0.029$), 83% mean reduction in TNF-alpha levels ($p=0.049$), 53% mean reduction in IL-17 levels ($p=0.005$), and 52% mean reduction in infiltrating monocytes/macrophages ($p=0.009$). MPC-treated animals had a 31% mean reduction in histopathology severity scores compared with controls ($p=0.025$). Intermediate effects were seen with 1 million MPCs/kg, and the lowest MPC dose was least effective. These findings demonstrate that MPCs are immunoregulatory and concomitantly suppress the activation and proliferation of T-cells, monocytes, and synoviocytes seen in active Rheumatoid Arthritis. Mechanistically, the data suggest that MPCs inhibit the Th17 CD4 T cell subset, with the subsequent simultaneous reduction in the key cytokines, IL-17, IL-6, and TNF-alpha.

Mesoblast has an upcoming scheduled meeting with the United States Food and Drug Administration (FDA) to discuss its Phase 2 clinical program in patients with RA. Subject to FDA clearance, the Company intends to commence a randomized, placebo-controlled Phase 2 trial in the fourth quarter of 2012.

"Rheumatoid Arthritis represents the second indication, after Type 2 diabetes, in a growing list of major market segments that will be targeted by Mesoblast's intravenous product formulation," Professor Itescu added.

About Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic systemic disease characterized by progressive joint deformity and joint destruction driven by synovial inflammation and hyperplasia in which cytokines play central pathogenic roles. The prevalence of RA is estimated to be 0.8% worldwide, with women twice as likely to develop the disease as men. In the United States, RA afflicts 1.3 million people. It is responsible for 250,000 hospitalizations and 9 million physician visits each year. According to Global Data, the RA therapeutics market was valued at $10.3 billion globally in 2010, and has doubled over a four-year period after growing at a Compound Annual Growth Rate (CAGR) of 12.3%.

About Mesoblast

Mesoblast Limited (ASX: MSB) is a world leader in commercialising biologic products for the broad field of regenerative medicine. Mesoblast has the worldwide exclusive rights for a series of patents and technologies developed over more than 10 years relating to the identification, extraction, culture and uses of adult Mesenchymal Precursor Cells (MPCs). www.mesoblast.com

mesoblast
the regenerative medicine company

asx announcement

For further information, please contact:
Julie Meldrum
Corporate Communications
Mesoblast Limited
T: + 61 (0) 3 9639 6036
E: julie.meldrum@mesoblast.com